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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,261	08/27/2003	Raymond Kim	20144-003100US	6593

20350 7590 09/26/2005

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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,261	KIM, RAYMOND	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/25/05, 11/24/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in the reply filed on June 27, 2005 is acknowledged. Claims 1-13 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being nõ allowable generic or linking claim. Claims 14-26 are under consideration in this office action.

Specification

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

3. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are drawn to an apparatus, however claim 26 does not provide any additional structural limitations to the apparatus, rather it is drawn to using mass spectrometry to detect the detectable product. Therefore the claim is objected to and clarification is required to overcome the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase drawn to an "environment that is unique within the film layer" in the claim is a relative phrase which renders the claim indefinite. The term "unique" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of uniqueness, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of how to define unique is unclear. Moreover, it is unclear how the additional zone is to comprise the same chemical or physical environment that is supposed to be unique within the film layer. It is unclear how to determine or define what the unique chemical or physical environment is and how to determine if the additional zone has such features. Therefore, clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 14-22 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Greenquist (US Patent 4,806,312 published February 21,1989).

The claims are drawn to an apparatus comprising a molecular analyte layer and a film layer wherein the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support, wherein said molecular analyte comprises a molecular ligand binding site; and (ii) the film layer comprises a molecular ligand zone having a molecular ligand, wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product. The dependant claims are drawn to using donor-acceptor pairs, enzymes and enzyme substrates, capture agents and the apparatus having multiple zones.

Greenquist teaches a multizone test device which provides a specific binding assay in a zoned or layered test strip or device (col. 5, lines 29-31). The labeled reagent is incorporated within the device, by being retained in the reagent zone and is free to migrate into the detection zone and capable of being bound to the immobilized interactive detection reagent in the detection zone (col. 5, lines 31-40). The reagent layer is incorporated with a reagent which comprises an immobilized form of the analyte (col. 5, lines 57-61). The labeled reagent can be prebound to the separate reagent zone, since the binding is reversible upon the addition of liquid test medium (col. 10, lines 12-20). The device utilizes

multiple reagent layers which can be prepared using film formers (col. 17, lines 4-9); thereby teaching a unique film layer, just as required by the claims. The reagent layer is equivalent to the film layer since both the reagent layer and the film layer have an immobilized molecule, as required by the claims. The detection layer is incorporated with an immobilized form of an interactive detection reagent (col. 5, lines 62-65). The detection layer is equivalent to the molecular analyte layer of the instant claims. Both the detection layer and the molecular analyte layer have an immobilized analyte on a solid support. The immobilizable material can be situated in any convenient location (col. 16, lines 54-65), thus the teaching embraces an array format just as claimed. The various layers of the multilayer device can be self-supporting and positioned onto a support member (col. 12, lines 32-39).

The labeled reagent can be a labeled form of a binding partner of the analyte and the immobilized reagent will be selected to be an immobilized form of the analyte (col. 5, lines 48-51). Therefore the labeled form of a binding partner of the analyte is equivalent to the molecular ligand found on the film layer (reagent layer) and the immobilized analyte detection reagent on the detection layer is equivalent to the molecular analyte immobilized on the molecular analyte layer. The analyte can be a peptide, protein nucleic acid or other molecule for which a specific binding partner or counterpart exist (col. 17, lines 30-36). It is noted, that the terms molecular analyte and molecular ligand are interchangeable with the terms labeled reagent and detection reagent used by Greenquist, since both pairs refer to binding partners and their counterparts.

The labeled reagent is permitted to diffuse and permeate into and through the reagent layer and into the detection layer and preferably provides only one available binding site for binding of the analyte to the labeled reagent (col. 6, lines (col. 6, lines 26-19 and 37-40). The labeled reagent can comprise the analyte labeled with a chemical group having a detectable chemical or interactive property (col. 7, lines 13-15). The chemical group does not generate a detectable product or provide a detectable signal prior to interacting with an appropriate interactive detection reagent (col. 7, lines 17-19). Representative chemical groups include enzymatically active groups such as enzymes, enzyme substrates, specifically bindable ligands and energy transfer pairs (col. 8, lines 4-16). The energy transfer pairs are also known as donor-acceptor pairs, just as required by the claims. For example, the label of the labeled reagent is an enzyme substrate and the immobilized detection reagent is an enzyme capable upon interaction with the substrate of producing a detectable product (col. 8, lines 26-35). Also, specifically binding ligand labeled species such as biotin can be detected by adding an antibody to the hapten or protein (avidin) which binds the ligand tagged or labeled with a detectable molecule (col. 8, lines 20-25). Thereby acting as protein immobilized capture agents, just as required by the claims. Such detectable molecules can produce measurable physical properties such as fluorescence or absorbance using the appropriate instrumentation (col. 8, lines 25-26). Thus, the interaction between the labeled reagent and the interactive detection reagent can inherently provide a detectable signal or require interaction with an additional substance to provide a detectable signal (col. 8, lines 57-63).

The various layers of the multilayer device may comprise additional layers which are known to enhance or modulate the performance of the device (col. 14, lines 15-21). For example spreading layers, intermediate layers, timing layers and additional reagent or detection layers have been taught (co. 14, lines 21-59). The various layers may comprise a porous matrix wherein matrix materials include various porous fibrous materials or matrix forming materials of various layers of the multilayer device wherein such materials are made of agarose or the like (col. 15, lines 35-55). Therefore the zones can be comprised of porous materials just as required by the claims. Figures 4 and 5 show additional zones below the molecular ligand zone (detection zone) just as required by the claims.

Thus, Greenquist teaches an apparatus comprising a molecular analyte layer and a film layer wherein the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support, wherein said molecular analyte comprises a molecular ligand binding site; and (ii) the film layer comprises a molecular ligand zone having a molecular ligand, wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenquist (US Patent 4,806,312 published February 21,1989) in view of Bergstrom et al., (US 5,436,161 published July, 1995).

The claims are drawn to the molecular ligand zone of the apparatus comprising a ligand within a hydrogel comprised of agarose. Greenquist has been discussed above, however Greenquist does not teach the use of a hydrogel comprised of agarose.

Bergstrom et al., teach a hydrogel matrix coating sensing surfaces capable of selective biomolecular interaction to be used with biosensing devices (col. 1, lines 52-56). Biocompatible porous matrixes, like hydrogel can be bound to the film layer or solid support (col. 5, lines 49-52). Hydrogel coupling is essential for obtaining a sensing surface and is desirable for aiding protein compatibility and minimizing nonspecific interactions (col. 5, lines 52-55). The hydrogel can be made from agarose or organic polymers such as poly-acrylamide materials (col. 5 lines 60-67).

Therefore, no more than routine skill would have been required to modify the apparatus of Greenquist to further incorporate hydrogel comprised of agarose

as taught by Bergstrom et al., since the art already teaches that the layers of the apparatus may be of matrix forming agarose materials. One would have a reasonable expectation of success because no more than routine skill would have been required to use a known member of a class of materials such as hydrogel in a apparatus since other members of matrix forming materials comprised of agarose were known to be useful for the purpose of forming layers within the apparatus. No more that routine skill would have been required in using a well known alternative and functionally equivalent material which is known in the art to be essential for obtaining a sensing surface and is desirable for aiding protein compatibility and minimizing nonspecific interactions. Moreover, hydrogel and other matrix forming materials are well known in the art to be used for comprising desired molecules and coating those molecules onto a film layered solid surface.

7. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Greenquist (US Patent 4,806,312 published February 21,1989) in view of Nelson et al., (1995. Ana. Chem).

The claim is drawn to the apparatus wherein the detectable product is detected by mass spectrometry. Greenquist has been discussed above, however Greenquist does not teach detection by mass spectrometry.

Nelson et al., teach detection of antigens by Matrix Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOFMS) (page 1153). Mass spectrometric immunoassay (MSIA) principles are taught by the

authors (page 1153). Immunoaffinity capture and mass spectrometry are separate yet have complementary roles during Mass spectrometric immunoassay (page 1153). Affinity capture is necessary to overcome signal suppression and matrix saturation effects typically encountered during direct MALDI analysis of complex biofluids and to increase molar sensitivity by concentration the antigen into a small volume (page 1153). Mass spectrometry is used for rapid, sensitive and highly specific detection of the affinity captured species (page 1154). Moreover, the most obvious benefit is the ability to screen for multiple antigens in a single assay (page 1154). Using MSIA reagents prepared with multiple antibodies, a number of antigens can be retrieved from solution and unambiguously determined in a single mass spectrum (page 1154). The multiple antigen analysis affords a dimension of specificity beyond that of conventional assays (page 1157).

It would have been prima facie obvious at the time applicants' invention to modify the apparatus of Greenquist to incorporate mass spectrometry detection as taught by Nelson et al., because the prior art already teach the use of antibodies to capture antigen and detect them using mass spectrometry. One would have a reasonable expectation of success because no more than routine skill would have been required to incorporate an antibody to detect an antigen when antibodies are well known in the art to capture antigens and be used in conjunction with the MALDI-TOF/mass spectrometry analysis. No more than routine skill is required to use the mass spectrometry techniques, since MSIA has high-level specificity offering a high level of immunity to ambiguities

arising from nonbiospecific adsorption. Moreover, the incorporation of mass spectrometry is desirable based on the fact that immunoaffinity capture and mass spectrometry have complementary roles; affinity capture is necessary to overcome signal suppression; increases molar sensitivity by concentration the antigen into a small volume; and is known for rapid, sensitive and highly specific detection of the affinity captured species.

Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wilding et al., (US Patent 5,866,345) teach analyte detection region is provided with a binding moiety immobilized with a specific binding moiety. Internal surfaces of the detection region may be coated with an immobilized binding moiety to enable the surface to interact with a fluid sample in order to detect specific fluid constituent. Wilding et al., refer to the detection region, also known as a capture zone, however both have at least one immobilized binding agent which complexes with the analyte to allow detection, thus the detection region meets the limitations of the claim. Antibodies, polynucleotide probes, ligands, or receptors may be immobilized on the surface as binding agents. The detection of analytes can be implemented by selecting the appropriate binding moiety coated on the surface of the detection region. Detection can occur using enzymes, optical means and mass spectroscopy.

Tsien et al., (WO 98/06737) fluorescent molecules are attractive as reporter molecules in many assay systems because of their high sensitivity and ease of quantification in immuno-detection assays. Fluorescence resonance energy transfer comprising a donor molecule and acceptor molecules for the fluorescent protein brings the donor molecule and the acceptor molecule into sufficiently close contact to allow fluorescence resonance energy transfer. The label can refer to a composition detectable by spectroscopic means using fluorescent dyes and fluorescent protein. The engineered fluorescent protein can be coupled to receptors for use in detection assays.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
August 30, 2005